

SEQUENCE LISTING

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Downes, Peter
Casamayor, Antonio

<120> Enzyme

<130> 002.00170

<140> US 09/937,009

<141> 2000-03-17

<150> PCT/GB00/01004

<151> 2000-03-17

<150> GB 9906245.7

<151> 1999-03-19

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<170> PatentIn Ver. 2.1

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<213> Homo sapiens

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5

10

15

Phe Asp Tyr Ile Ala Asp Trp Cys

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peptide sequence that interacts with human PRK2
region B

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Phe Asp Tyr Ile Ala Asp Trp Cys
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peptide sequence that interacts with human PRK2
region B

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Phe Asp Tyr Ile Ala Asp Trp Cys
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<210> 4

<211> 53

<212> PRT

<213> Homo sapiens

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Arg Glu Asp Val Ser Asn Phe Asp Asp Glu Phe Thr Ser Glu Ala Pro
35 40 45

<210> 8
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<212> PRT
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<220>
<223> region of PKB alpha

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<220>
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Thr Phe Cys Gly Thr Pro Glu Phe Leu
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<212> PRT
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<220>
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<210> 11
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<213> Artificial Sequence

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substrate peptide

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Glu Asp Val Lys Lys His Pro Phe Phe Arg Leu Ile Asp Trp Ser Ala
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Leu Met Asp Lys Lys Val Lys Pro Pro Phe Ile Pro Thr Ile Arg Gly
20 25 30

Arg Glu Asp Val Ser Asn Phe Asp Asp Glu Phe Thr Ser Glu Ala Pro
35 40 45

Ile Leu Thr Pro Pro Arg Glu Pro Arg Ile Leu Ser Glu Glu Gln
 50 55 60

Glu Met Phe Arg Asp Phe Asp Tyr Ile Ala Asp Trp Cys
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 20 25 30

Arg Thr Asp Val Ser Asn Phe Asp Glu Glu Phe Thr Gly Glu Ala Pro
 35 40 45

Thr Leu Ser Pro Pro Arg Asp Ala Arg Pro Leu Thr Ala Ala Glu Gln
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Ala Ala Phe Leu Asp Phe Asp Phe Val Ala Gly Gly Cys
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Val Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser
 20 25 30

<220>

<223> region of PKC alpha

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Arg Asp Val Arg Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys
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 20 25 30
 Lys Gly Ala Glu Asn Phe Asp Lys Phe Phe Thr Arg Gly Gln Pro Val .
 35 40 45
 Leu Thr Pro Pro Asp Gln Leu Val Ile Ala Asn Ile Asp Gln Ser Asp
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<211> 62

<212> PRT

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 35 40 45
 Val Ser Ile Thr Glu Cys Ala Lys Glu Lys Phe Gly Glu Phe
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<223> PKB consensus sequence

<220>

<223> residues 2 and 3 are variable amino acids

<400> 22

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1 5

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Thr Phe Cys Gly Thr Xaa Glu Leu

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<223> residues 2 and 3 are variable amino acids

<220>

<223> residue 5 is serine or threonine

<220>

<223> residue 6 is phenylalanine or tyrosine

<400> 24

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1 5

<210> 25
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<220>
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 sequence that interacts with PKB

<220>
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<220>
 <223> residues 1, 4 and 6 are phenylalanine or tyrosine

<220>
 <223> residue 5 is a negatively charged amino acid

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 1 5

<210> 26
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 <223> residues 1, 4 and 6 are phenylalanine or tyrosine

<220>
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<400> 26
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<210> 27
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 sequence that interacts with PKB

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<400> 27
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<210> 28
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<220>
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 Xaa Phe Cys Gly Thr Xaa Glu Leu
 1 5

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<212> PRT

<213> Homo sapiens

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<223> PRK2 sequence

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20 25 30

Lys Leu Asp Phe Ser Asp Thr Met Val Gln Gln Lys Leu Asp Asp Ile
35 40 45

Lys Asp Arg Ile Lys Arg Glu Ile Arg Lys Glu Leu Lys Ile Lys Glu
50 55 60

Gly Ala Glu Asn Leu Arg Lys Val Thr Thr Asp Lys Lys Ser Leu Ala
65 70 75 80

Tyr Val Asp Asn Ile Leu Lys Lys Ser Asn Lys Lys Leu Glu Glu Leu
85 90 95

His His Lys Leu Gln Glu Leu Asn Ala His Ile Val Val Ser Asp Pro
100 105 110

Glu Asp Ile Thr Asp Cys Pro Arg Thr Pro Asp Thr Pro Asn Asn Asp
115 120 125

Pro Arg Cys Ser Thr Ser Asn Asn Arg Leu Lys Ala Leu Gln Lys Gln
130 135 140

Leu Asp Ile Glu Leu Lys Val Lys Gln Gly Ala Glu Asn Met Ile Gln
145 150 155 160

Met Tyr Ser Asn Gly Ser Ser Lys Asp Arg Lys Leu His Gly Thr Ala
165 170 175

Gln Gln Leu Leu Gln Asp Ser Lys Thr Lys Ile Glu Val Ile Arg Met
180 185 190

Gln Ile Leu Gln Ala Val Gln Thr Asn Glu Leu Ala Phe Asp Asn Ala
195 200 205

Lys Pro Val Ile Ser Pro Leu Glu Leu Arg Met Glu Glu Leu Arg His
210 215 220

$\frac{1}{\sqrt{\pi}} \int_{-\infty}^{\infty} f(x) \delta(x-a) dx = f(a)$

His	Phe	Arg	Ile	Glu	Phe	Ala	Val	Ala	Glu	Gly	Ala	Lys	Asn	Val	Met	
225					230					235					240	
Lys	Leu	Leu	Gly	Ser	Gly	Lys	Val	Thr	Asp	Arg	Lys	Ala	Leu	Ser	Glu	
245					250					255						
Ala	Gln	Ala	Arg	Phe	Asn	Glu	Ser	Ser	Gln	Lys	Leu	Asp	Leu	Leu	Lys	
260					265					270						
Tyr	Ser	Leu	Glu	Gln	Arg	Leu	Asn	Glu	Val	Pro	Lys	Asn	His	Pro	Lys	
275					280					285						
Ser	Arg	Ile	Ile	Ile	Glu	Glu	Leu	Ser	Leu	Val	Ala	Ala	Ser	Pro	Thr	
290					295					300						
Leu	Ser	Pro	Arg	Gln	Ser	Met	Ile	Ser	Thr	Gln	Asn	Gln	Tyr	Ser	Thr	
305					310					315					320	
Leu	Ser	Lys	Pro	Ala	Ala	Leu	Thr	Gly	Thr	Leu	Glu	Val	Arg	Leu	Met	
325					330					335						
Gly	Cys	Gln	Asp	Ile	Leu	Glu	Asn	Val	Pro	Gly	Arg	Ser	Lys	Ala	Thr	
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Ser	Val	Ala	Leu	Pro	Gly	Trp	Ser	Pro	Ser	Glu	Thr	Arg	Ser	Ser	Phe	
355					360					365						
Met	Ser	Arg	Thr	Ser	Lys	Ser	Lys	Ser	Gly	Ser	Ser	Arg	Asn	Leu	Leu	
370					375					380						
Lys	Thr	Asp	Asp	Leu	Ser	Asn	Asp	Val	Cys	Ala	Val	Leu	Lys	Leu	Asp	
385					390					395					400	
Asn	Thr	Val	Val	Gly	Gln	Thr	Ser	Trp	Lys	Pro	Ile	Ser	Asn	Gln	Ser	
405					410					415						
Trp	Asp	Gln	Lys	Phe	Thr	Leu	Glu	Leu	Asp	Arg	Ser	Arg	Glu	Leu	Glu	
420					425					430						
Ile	Ser	Val	Tyr	Trp	Arg	Asp	Trp	Arg	Ser	Leu	Cys	Ala	Val	Lys	Phe	
435					440					445						
Leu	Arg	Leu	Glu	Asp	Phe	Leu	Asp	Asn	Gln	Arg	His	Gly	Met	Cys	Leu	
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Tyr	Leu	Glu	Pro	Gln	Gly	Thr	Leu	Phe	Ala	Glu	Val	Thr	Phe	Phe	Asn	
465					470					475					480	

Pro	Val	Ile	Glu	Arg	Arg	Pro	Lys	Leu	Gln	Arg	Gln	Lys	Lys	Ile	Phe						
				485								490								495	
Ser	Lys	Gln	Gln	Gly	Lys	Thr	Phe	Leu	Arg	Ala	Pro	Gln	Met	Asn	Ile						
				500								505								510	
Asn	Ile	Ala	Thr	Trp	Gly	Arg	Leu	Val	Arg	Arg	Ala	Ile	Pro	Thr	Val						
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Asn	His	Ser	Gly	Thr	Phe	Ser	Pro	Gln	Ala	Pro	Val	Pro	Thr	Thr	Val						
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Pro	Val	Val	Asp	Val	Arg	Ile	Pro	Gln	Leu	Ala	Pro	Pro	Ala	Ser	Asp						
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Ser	Thr	Val	Thr	Lys	Leu	Asp	Phe	Asp	Leu	Glu	Pro	Glu	Pro	Pro	Pro						
				565								570								575	
Ala	Pro	Pro	Arg	Ala	Ser	Ser	Leu	Gly	Glu	Ile	Asp	Glu	Ser	Ser	Glu						
				580								585								590	
Leu	Arg	Val	Leu	Asp	Ile	Pro	Gly	Gln	Asp	Ser	Glu	Thr	Val	Phe	Asp						
				595								600								605	
Ile	Gln	Asn	Asp	Arg	Asn	Ser	Ile	Leu	Pro	Lys	Ser	Gln	Ser	Glu	Tyr						
				610								615								620	
Lys	Pro	Asp	Thr	Pro	Gln	Ser	Gly	Leu	Glu	Tyr	Ser	Gly	Ile	Gln	Glu						
625								630								635				640	
Leu	Glu	Asp	Arg	Arg	Ser	Gln	Gln	Arg	Phe	Gln	Phe	Asn	Leu	Gln	Asp						
				645								650								655	
Phe	Arg	Cys	Cys	Ala	Val	Leu	Gly	Arg	Gly	His	Phe	Gly	Lys	Val	Leu						
				660								665								670	
Leu	Ala	Glu	Tyr	Lys	Asn	Thr	Asn	Glu	Met	Phe	Ala	Ile	Lys	Ala	Leu						
				675								680								685	
Lys	Lys	Gly	Asp	Ile	Val	Ala	Arg	Asp	Glu	Val	Asp	Ser	Leu	Met	Cys						
690								695								700					
Glu	Lys	Arg	Ile	Phe	Glu	Thr	Val	Asn	Ser	Val	Arg	His	Pro	Phe	Leu						
705								710								715				720	
Val	Asn	Leu	Phe	Ala	Cys	Phe	Gln	Thr	Lys	Glu	His	Val	Cys	Phe	Val						
				725								730								735	

$$\frac{1}{\Gamma(\alpha)} \int_0^t (t-\tau)^{\alpha-1} f(\tau) d\tau = I^\alpha f(t), \quad t \geq 0, \quad (1)$$

Met Glu Tyr Ala Ala Gly Gly Asp Leu Met Met His Ile His Thr Asp
740 745 750

Val Phe Ser Glu Pro Arg Ala Val Phe Tyr Ala Ala Cys Val Val Leu
755 760 765

Gly Leu Gln Tyr Leu His Glu His Lys Ile Val Tyr Arg Asp Leu Lys
770 775 780

Leu Asp Asn Leu Leu Leu Asp Thr Glu Gly Phe Val Lys Ile Ala Asp
785 790 795 800

Phe Gly Leu Cys Lys Glu Gly Met Gly Tyr Gly Asp Arg Thr Ser Thr
805 810 815

Phe Cys Gly Thr Pro Glu Phe Leu Ala Pro Glu Val Leu Thr Glu Thr
820 825 830

Ser Tyr Thr Arg Ala Val Asp Trp Trp Gly Leu Gly Val Leu Ile Tyr
835 840 845

Glu Met Leu Val Gly Glu Ser Pro Phe Pro Gly Asp Asp Glu Glu Glu
850 855 860

Val Phe Asp Ser Ile Val Asn Asp Glu Val Arg Tyr Pro Arg Phe Leu
865 870 875 880

Ser Thr Glu Ala Ile Ser Ile Met Arg Arg Leu Leu Arg Arg Asn Pro
885 890 895

Glu Arg Arg Leu Gly Ala Ser Glu Lys Asp Ala Glu Asp Val Lys Lys
900 905 910

His Pro Phe Phe Arg Leu Ile Asp Trp Ser Ala Leu Met Asp Lys Lys
915 920 925

Val Lys Pro Pro Phe Ile Pro Thr Ile Arg Gly Arg Glu Asp Val Ser
930 935 940

Asn Phe Asp Asp Glu Phe Thr Ser Glu Ala Pro Ile Leu Thr Pro Pro
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Phe Asp Tyr Ile Ala Asp Trp Cys
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<220>
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Gln Gln Leu Glu Leu Glu Arg Glu Arg Leu Arg Arg Glu Ile Arg Lys
          35             40             45
Glu Leu Lys Leu Lys Glu Gly Ala Glu Asn Leu Arg Arg Ala Thr Thr
          50             55             60
Asp Leu Gly Arg Ser Leu Gly Pro Val Glu Leu Leu Leu Arg Gly Ser
  65             70             75             80
Ser Arg Arg Leu Asp Leu Leu His Gln Gln Leu Gln Glu Leu His Ala
          85             90             95
His Val Val Leu Pro Asp Pro Ala Ala Thr His Asp Gly Pro Gln Ser
          100             105             110
Pro Gly Ala Gly Gly Pro Thr Cys Ser Ala Thr Asn Leu Ser Arg Val
          115             120             125
Ala Gly Leu Glu Lys Gln Leu Ala Ile Glu Leu Lys Val Lys Gln Gly
          130             135             140
Ala Glu Asn Met Ile Gln Thr Tyr Ser Asn Gly Ser Thr Lys Asp Arg
  145             150             155             160
Lys Leu Leu Leu Thr Ala Gln Gln Met Leu Gln Asp Ser Lys Thr Lys
          165             170             175
Ile Asp Ile Ile Arg Met Gln Leu Arg Arg Ala Leu Gln Ala Asp Gln
          180             185             190
Leu Glu Asn Gln Ala Ala Pro Asp Asp Thr Gln Gly Ser Pro Asp Leu

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195	200	205
Gly Ala Val Glu Leu Arg	Ile Glu Glu Leu Arg	His His Phe Arg Val
210	215	220
Glu His Ala Val Ala Glu	Gly Ala Lys Asn Val	Leu Arg Leu Leu Ser
225	230	235 240
Ala Ala Lys Ala Pro Asp	Arg Lys Ala Val Ser	Glu Ala Gln Glu Lys
	245	250 255
Leu Thr Glu Ser Asn Gln	Lys Leu Gly Leu Leu Arg	Glu Ala Leu Glu
	260	265 270
Arg Arg Leu Gly Glu Leu	Pro Ala Asp His Pro Lys	Gly Arg Leu Leu
	275	280 285
Arg Glu Glu Leu Ala Ala	Ala Ser Ser Ala Ala Phe	Ser Thr Arg Leu
	290	295 300
Ala Gly Pro Phe Pro Ala	Thr His Tyr Ser Thr Leu	Cys Lys Pro Ala
305	310	315 320
Pro Leu Thr Gly Thr Leu	Glu Val Arg Val Val Gly	Cys Arg Asp Leu
	325	330 335
Pro Glu Thr Ile Pro Trp	Asn Pro Thr Pro Ser Met	Gly Gly Pro Gly
	340	345 350
Thr Pro Asp Ser Arg Pro	Pro Phe Leu Ser Arg Pro	Ala Arg Gly Leu
	355	360 365
Tyr Ser Arg Ser Gly Ser	Leu Ser Gly Arg Ser Ser	Leu Lys Ala Glu
	370	375 380
Ala Glu Asn Thr Ser Glu	Val Ser Thr Val Leu Lys	Leu Asp Asn Thr
385	390	395 400
Val Val Gly Gln Thr Ser	Trp Lys Pro Cys Gly Pro	Asn Ala Trp Asp
	405	410 415
Gln Ser Phe Thr Leu Glu	Leu Glu Arg Ala Arg Glu	Leu Glu Leu Ala
	420	425 430
Val Phe Trp Arg Asp Gln	Arg Gly Leu Cys Ala Leu	Lys Phe Leu Lys
	435	440 445
Leu Glu Asp Phe Leu Asp	Asn Glu Arg His Glu Val	Gln Leu Asp Met

705					710					715					720					
Ser	Ala	Cys	Val	Val	Leu	Gly	Leu	Gln	Phe	Leu	His	Glu	His	Lys	Ile					
				725					730					735						
Val	Tyr	Arg	Asp	Leu	Lys	Leu	Asp	Asn	Leu	Leu	Leu	Asp	Thr	Glu	Gly					
				740					745					750						
Tyr	Val	Lys	Ile	Ala	Asp	Phe	Gly	Leu	Cys	Lys	Glu	Gly	Met	Gly	Tyr					
				755					760					765						
Gly	Asp	Arg	Thr	Ser	Thr	Phe	Cys	Gly	Thr	Pro	Glu	Phe	Leu	Ala	Pro					
				770					775					780						
Glu	Val	Leu	Thr	Asp	Thr	Ser	Tyr	Thr	Arg	Ala	Val	Asp	Trp	Trp	Gly					
785					790					795					800					
Leu	Gly	Val	Leu	Leu	Tyr	Glu	Met	Leu	Val	Gly	Glu	Ser	Pro	Phe	Pro					
				805					810					815						
Gly	Asp	Asp	Glu	Glu	Glu	Val	Phe	Asp	Ser	Ile	Val	Asn	Asp	Glu	Val					
				820					825					830						
Arg	Tyr	Pro	Arg	Phe	Leu	Ser	Ala	Glu	Ala	Ile	Gly	Ile	Met	Arg	Arg					
				835					840					845						
Leu	Leu	Arg	Arg	Asn	Pro	Glu	Arg	Arg	Leu	Gly	Ser	Ser	Glu	Arg	Asp					
				850					855					860						
Ala	Glu	Asp	Val	Lys	Lys	Gln	Pro	Phe	Phe	Arg	Thr	Leu	Gly	Trp	Glu					
865					870					875					880					
Ala	Leu	Leu	Ala	Arg	Arg	Leu	Pro	Pro	Pro	Phe	Val	Pro	Thr	Leu	Ser					
				885					890					895						
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				900					905					910						
Pro	Thr	Leu	Ser	Pro	Pro	Arg	Asp	Ala	Arg	Pro	Leu	Thr	Ala	Ala	Glu					
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Ile	Lys	Ile	Ser	Gln	Gly	Leu	Gly	Leu	Gln	Asp	Phe	Asp	Leu	Ile	Arg
				245					250					255	
Val	Ile	Gly	Arg	Gly	Thr	Tyr	Ala	Lys	Val	Leu	Leu	Val	Arg	Leu	Lys
			260					265					270		
Lys	Asn	Asp	Gln	Ile	Tyr	Ala	Met	Lys	Val	Val	Lys	Lys	Glu	Leu	Val
		275					280					285			
His	Asp	Asp	Glu	Asp	Ile	Asp	Trp	Val	Gln	Thr	Glu	Lys	His	Val	Phe
	290					295					300				
Glu	Gln	Ala	Ser	Ser	Asn	Pro	Phe	Leu	Val	Gly	Leu	His	Ser	Cys	Phe
305					310					315					320
Gln	Thr	Thr	Ser	Arg	Leu	Phe	Leu	Val	Ile	Glu	Tyr	Val	Asn	Gly	Gly
				325					330					335	
Asp	Leu	Met	Phe	His	Met	Gln	Arg	Gln	Arg	Lys	Leu	Pro	Glu	Glu	His
			340					345					350		
Ala	Arg	Phe	Tyr	Ala	Ala	Glu	Ile	Cys	Ile	Ala	Leu	Asn	Phe	Leu	His
		355					360					365			
Glu	Arg	Gly	Ile	Ile	Tyr	Arg	Asp	Leu	Lys	Leu	Asp	Asn	Val	Leu	Leu
	370					375					380				
Asp	Ala	Asp	Gly	His	Ile	Lys	Leu	Thr	Asp	Tyr	Gly	Met	Cys	Lys	Glu
385					390					395					400
Gly	Leu	Gly	Pro	Gly	Asp	Thr	Thr	Ser	Thr	Phe	Cys	Gly	Thr	Pro	Asn
				405					410					415	
Tyr	Ile	Ala	Pro	Glu	Ile	Leu	Arg	Gly	Glu	Glu	Tyr	Gly	Phe	Ser	Val
			420					425					430		
Asp	Trp	Trp	Ala	Leu	Gly	Val	Leu	Met	Phe	Glu	Met	Met	Ala	Gly	Arg
		435					440					445			
Ser	Pro	Phe	Asp	Ile	Ile	Thr	Asp	Asn	Pro	Asp	Met	Asn	Thr	Glu	Asp
	450					455					460				
Tyr	Leu	Phe	Gln	Val	Ile	Leu	Glu	Lys	Pro	Ile	Arg	Ile	Pro	Arg	Phe
465					470					475					480

[illegible]

Leu Ser Val Lys Ala Ser His Val Leu Lys Gly Phe Leu Asn Lys Asp
485 490 495

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500 505 510

Lys Ser His Ala Phe Phe Arg Ser Ile Asp Trp Asp Leu Leu Glu Lys
515 520 525

Lys Gln Ala Leu Pro Pro Phe Gln Pro Gln Ile Thr Asp Asp Tyr Gly
530 535 540

Leu Asp Asn Phe Asp Thr Gln Phe Thr Ser Glu Pro Val Gln Leu Thr
545 550 555 560

Pro Asp Asp Glu Asp Ala Ile Lys Arg Ile Asp Gln Ser Glu Phe Glu
565 570 575

Gly Phe Glu Tyr Ile Asn Pro Leu Leu Leu Ser Thr Glu Glu Ser Val
580 585 590